Cardiovascular events in users of sildenafil: results from first phase of prescription event monitoring in England

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Sildenafil is used to treat erectile dysfunction, and prescription on the NHS is restricted. We are conducting a study of prescription event monitoring for sildenafil in England, the first phase of which investigates possible short term effects in a cohort of about 5000 users. In view of the interest in myocardial infarction as a possible short term side effect[1] we report on an analysis of selected cardiovascular events reported in the first phase.

Methods and results

Prescription event monitoring has been described elsewhere.[2] Patients were identified from NHS prescriptions in England. Simple questionnaires were posted to the prescribing general practitioners about five months after the first prescription. These forms requested reporting of events after the drug had been prescribed. An "event" was any new diagnosis, any reason for referral to a consultant or admission to hospital, unexpected deterioration (or improvement) in a concurrent illness, suspected drug reaction, clinically important alterations in laboratory measurements or other investigations, or any other complaint considered to be of sufficient importance to enter in the patient's notes.

We sent questionnaires for 9748 patients who were first prescribed sildenafil between September 1998 and March 1999. Of the 5950 questionnaires returned, 5601 contained usable information. The mean (SD) age of the patients was 57.4 (11.3) years (range 18-90 years). The main indication for use of sildenafil was impotence (3552; 63.4%); the indication was not specified in 1927 (34.4%). Diabetes mellitus was the second indication in 789 (14.1%), and in 39 (0.7%) it was the primary indication. Eighty three patients had other first indications for treatment. The number of patients with diabetes may be an underestimate as data on more than one indication for treatment are not specifically requested. Three months after the first prescription 85.6% were still using the drug.

We followed up all patients with non-fatal myocardial infarction and selected patients with angina,

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Standardised mortality calculation for ischaemic heart disease/myocardial infarction. Figures are numbers for cohort unless stated otherwise

Age (years)	No of patients	Years of observation	No of deaths	No of deaths/year	Deaths/1000/ year in England (1998)	Expected No of deaths in cohort/year
15-24	15	0.55	0	0	0.003600	0.000054
25-34	145	0.51	0	0	0.028400	0.004118
35-44	473	0.49	0	0	0.222000	0.105006
45-54	1171	0.51	1.00	1.97	0.978100	1.145355
55-64	1583	0.50	5.00	10.00	3.277600	5.188440
65-74	1200	0.50	2.00	4.01	9.153800	10.984560
⩾75	190	0.48	2.00	4.21	60.278400	11.452896
Not specified	824	0.49	N/A	N/A	N/A	N/A
Total	5601	0.50	10.00	20.20	73.941900	28.88

ischaemic heart disease, and chest pain. In patients who were taking sildenafil non-fatal events were angina (nine), chest pain (19), ischaemic heart disease (five), and myocardial infarction (seven) and fatal events were myocardial infarction (six) and ischaemic heart disease (four). One death was certified as congestive cardiac failure/ischaemic heart disease after intercourse. Four of the 10 patients who died were known to have had diabetes.

We used indirect standardisation to compare mortality from ischaemic heart disease (ICD-9 (international classification of diseases, 9th revision) codes 410-414) in the cohort with that in the general population of England in 1998 (table).[3] The standardised mortality ratio of 69.9 (95% confidence interval 42.7 to 108.0, based on Poisson error factors) indicates that the mortality in the cohort is 30.1% lower than that for English men in 1998, after adjustment for confounding effects of age.

Comment

The standardised mortality ratio indicates no evidence for a higher incidence of fatal myocardial infarction or ischaemic heart disease among men taking sildenafil. Underreporting of adverse events is possible, and bias caused by non-response among general practitioners and NHS restrictions on prescribing sildenafil cannot be excluded. The prevalence of diabetes in the cohort was 15%, which is similar to that (16%) in the manufacturer's clinical trials[4] but much higher than that in the general population (3.3% in men in England in 1998).[5] Though our results are reassuring it is inappropriate to accept these comparisons as definitive evidence of equivalence between this cohort of sildenafil users and men in the general population in England. This hypothesis needs to be examined by further clinical and pharmacoepidemiological research.

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